

REMARKS

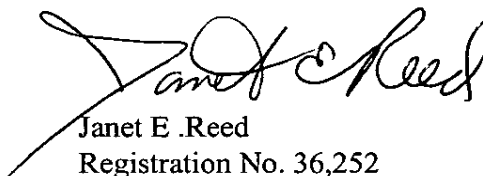
In response to a Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures issued March 21, 2002, Applicants submit herewith a paper copy and a computer-readable form of a Sequence Listing of all sequences disclosed in the above-referenced patent application. This preliminary amendment directs entry of the paper copy of the Sequence Listing into the specification.

In addition, amendments to the specification are made at page 8 and 10, to correct discrepancies in numbering of the Sequence ID Numbers.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

It is believed that the application is now in condition for examination on the merits.

Respectfully Submitted,

  
Janet E .Reed  
Registration No. 36,252

Date: 4/23/02

WOODCOCK WASHBURN LLP  
One Liberty Place - 46<sup>th</sup> Floor  
Philadelphia, PA 19103  
(215) 568-3100



DOCKET NO.: PU-0031 (01-1739-1)

PATENT

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The Sequence Listing shown below has been entered after the last page of the specification and before the first page of claims.

---

SEQUENCE LISTING

<110> Shi, Yigong  
<120> Compositions And Methods For Regulating Apoptosis  
<130> PU-0031 (01-1739-1)  
<140> 09/965,967  
<141> 2001-09-28  
<150> 60/236,574  
<151> 2000-09-29  
<150> 60/256,830  
<151> 2000-12-20  
<160> 30  
<170> PatentIn version 3.1  
<210> 1  
<211> 4  
<212> PRT  
<213> Homo sapiens  
<400> 1  
Ala Val Pro Ile  
1  
  
<210> 2  
<211> 4  
<212> PRT  
<213> Drosophila melanogaster  
<400> 2

**DOCKET NO.: PU-0031 (01-1739-1)**

**PATENT**

Ala Val Ala Phe

1

<210> 3

<211> 4

<212> PRT

<213> Drosophila melanogaster

<400> 3

Ala Ile Ala Tyr

1

<210> 4

<211> 4

<212> PRT

<213> Drosophila melanogaster

<400> 4

Ala Val Pro Phe

1

A1 <210> 5

<211> 4

<212> PRT

<213> Homo sapiens

<400> 5

Ala Thr Pro Phe

1

<210> 6

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Peptide

<400> 6

Ala Val Pro Tyr

1

<210> 7

**DOCKET NO.: PU-0031 (01-1739-1)**

**PATENT**

<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Peptide

<400> 7

Ala Thr Pro Val  
1

<210> 8  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 8

Ala Val Pro Ile Ala Gln Lys  
1 5

AI  
<210> 9  
<211> 7  
<212> PRT  
<213> Drosophila melanogaster

<400> 9

Ala Val Ala Phe Tyr Ile Pro  
1 5

<210> 10  
<211> 7  
<212> PRT  
<213> Drosophila melanogaster

<400> 10

Ala Ile Ala Tyr Phe Leu Pro  
1 5

<210> 11  
<211> 7  
<212> PRT  
<213> Drosophila melanogaster

**DOCKET NO.: PU-0031 (01-1739-1)**

**PATENT**

<400> 11

Ala Val Pro Phe Tyr Leu Pro  
1 5

<210> 12

<211> 7

<212> PRT

<213> Homo sapiens

<400> 12

Ala Thr Pro Phe Gln Glu Gly  
1 5

<210> 13

<211> 7

<212> PRT

<213> Mus musculus

<400> 13

Ala Val Pro Tyr Gln Glu Gly  
1 5

<210> 14

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Peptide

<400> 14

Ala Thr Pro Val Phe Ser Gly  
1 5

<210> 15

<211> 10

<212> PRT

<213> Drosophila melanogaster

<400> 15

Ala Val Pro Phe Tyr Leu Pro Glu Gly Gly  
1 5 10

<210> 16  
 <211> 10  
 <212> PRT  
 <213> Drosophila melanogaster

<400> 16

Ala Ile Ala Tyr Phe Ile Pro Asp Gln Ala  
 1 5 10

<210> 17  
 <211> 10  
 <212> PRT  
 <213> Drosophila melanogaster

<400> 17

Ala Val Ala Phe Tyr Ile Pro Asp Gln Ala  
 1 5 10

<210> 18  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 18

Ala Val Pro Ile Ala Gln Lys Ser Glu Pro  
 1 5 10

<210> 19  
 <211> 109  
 <212> PRT  
 <213> Drosophila melanogaster

<400> 19

Lys Asn Asn Ile Asn Lys Thr Arg Met Asn Asp Leu Asn Arg Glu Glu  
 1 5 10 15

Thr Arg Leu Lys Thr Phe Thr Asp Trp Pro Leu Asp Trp Leu Asp Lys  
 20 25 30

Arg Gln Leu Ala Gln Thr Gly Met Tyr Phe Thr His Ala Gly Asp Lys  
 35 40 45

DOCKET NO.: PU-0031 (01-1739-1)

PATENT

Val Lys Cys Phe Phe Cys Gly Val Glu Ile Gly Cys Trp Glu Gln Glu  
50 55 60

Asp Gln Pro Val Pro Glu His Gln Arg Trp Ser Pro Asn Cys Pro Leu  
65 70 75 80

Leu Arg Arg Arg Thr Thr Asn Asn Val Pro Ile Asn Ala Glu Ala Leu  
85 90 95

Asp Arg Ile Leu Pro Pro Ile Ser Tyr Asp Ile Cys Gly  
100 105

<210> 20  
<211> 107  
<212> PRT  
<213> Homo sapiens

<400> 20

Pro Asn Ser Thr Asn Leu Pro Arg Asn Pro Ser Met Ala Asp Tyr Glu  
1 5 10 15

Ala Arg Ile Phe Thr Phe Gly Thr Trp Ile Tyr Ser Val Asn Lys Glu  
20 25 30

Gln Leu Ala Arg Ala Gly Phe Tyr Ala Leu Gly Glu Gly Asp Lys Val  
35 40 45

Lys Cys Phe His Cys Gly Gly Gly Leu Thr Asp Trp Lys Pro Ser Glu  
50 55 60

Asp Pro Trp Glu Gln His Ala Lys Trp Tyr Pro Gly Cys Lys Tyr Leu  
65 70 75 80

Leu Glu Gln Lys Gly Gln Glu Tyr Ile Asn Asn Ile His Leu Thr His  
85 90 95

Ser Leu Glu Glu Cys Leu Val Arg Thr Thr Glu  
100 105

<210> 21

DOCKET NO.: PU-0031 (01-1739-1)

PATENT

<211> 110  
<212> PRT  
<213> Homo sapiens

<400> 21

Ile Ser Asp Thr Ile Tyr Pro Arg Asn Pro Ala Met Tyr Cys Glu Glu  
1 5 10 15

Ala Arg Leu Lys Ser Phe Gln Asn Trp Pro Asp Tyr Ala His Leu Thr  
20 25 30

Pro Arg Glu Leu Ala Ser Ala Gly Leu Tyr Tyr Thr Gly Ile Gly Asp  
35 40 45

Gln Val Gln Cys Phe Cys Cys Gly Gly Lys Leu Lys Asn Trp Glu Pro  
50 55 60

Cys Asp Arg Ala Trp Ser Glu His Arg Arg His Phe Pro Asn Cys Phe  
65 70 75 80

Phe Val Leu Gly Arg Asn Leu Asn Ile Arg Ser Glu Ser Asp Ala Val  
85 90 95

Ser Ser Asp Arg Asn Phe Pro Asn Ser Thr Asn Leu Pro Arg  
100 105 110

<210> 22  
<211> 110  
<212> PRT  
<213> Homo sapiens

<400> 22

Thr Cys Val Pro Ala Asp Ile Asn Lys Glu Glu Glu Phe Val Glu Glu  
1 5 10 15

Phe Asn Arg Leu Lys Thr Phe Ala Asn Phe Pro Ser Gly Ser Pro Val  
20 25 30

Ser Ala Ser Thr Leu Ala Arg Ala Gly Phe Leu Tyr Thr Gly Glu Gly  
35 40 45



DOCKET NO.: PU-0031 (01-1739-1)

PATENT

Asp Thr Val Arg Cys Phe Ser Cys His Ala Ala Val Asp Arg Trp Gln  
50 55 60

Tyr Gly Asp Ser Ala Val Gly Arg His Arg Lys Val Ser Pro Asn Cys  
65 70 75 80

Arg Phe Ile Asn Gly Phe Tyr Leu Glu Asn Ser Ala Thr Gln Ser Thr  
85 90 95

Asn Ser Gly Ile Gln Asn Gly Gln Tyr Lys Val Glu Asn Tyr  
100 105 110

<210> 23  
<211> 98  
<212> PRT  
<213> Homo sapiens

<400> 23

Met Gly Ala Pro Thr Leu Pro Pro Ala Trp Gln Pro Phe Leu Lys Asp  
1 5 10 15

His Arg Ile Ser Thr Phe Lys Asn Trp Pro Phe Leu Glu Gly Cys Ala  
20 25 30

Cys Thr Pro Glu Arg Met Ala Glu Ala Gly Phe Ile His Cys Pro Thr  
35 40 45

Glu Asn Glu Pro Asp Leu Ala Gln Cys Phe Phe Cys Phe Lys Glu Leu  
50 55 60

Glu Gly Trp Glu Pro Asp Asp Asp Pro Ile Glu Glu His Lys Lys His  
65 70 75 80

Ser Ser Gly Cys Ala Phe Leu Ser Val Lys Lys Gln Phe Glu Glu Leu  
85 90 95

Thr Leu

<210> 24

**DOCKET NO.: PU-0031 (01-1739-1)**

**PATENT**

<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 24

Met Val Pro Ile  
1

<210> 25  
<211> 13  
<212> PRT  
<213> Drosophila melanogaster

<400> 25

Met Thr Ser Ala Val Pro Ile Ala Gln Lys Ser Glu Pro  
1 5 10

A1  
<210> 26  
<211> 11  
<212> PRT  
<213> Drosophila melanogaster

<400> 26

Met Ala Val Pro Phe Tyr Leu Pro Glu Gly Gly  
1 5 10

<210> 27  
<211> 11  
<212> PRT  
<213> Drosophila melanogaster

<400> 27

Met Ala Val Ala Phe Tyr Ile Pro Asp Gln Ala  
1 5 10

<210> 28  
<211> 11  
<212> PRT  
<213> Drosophila melanogaster

<400> 28

Met Ala Ile Ala Tyr Phe Ile Pro Asp Gln Ala  
1 5 10

<210> 29  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Peptide

<220>  
 <221> misc\_feature  
 <222> (2)..(2)  
 <223> X is V, T, or I

<220>  
 <221> misc\_feature  
 <222> (3)..(3)  
 <223> X is P or A

<220>  
 <221> misc\_feature  
 <222> (4)..(4)  
 <223> X is F, Y, I, or V

<400> 29

Ala Xaa Xaa Xaa  
 1

<210> 30  
 <211> 109  
 <212> PRT  
 <213> Drosophila melanogaster

<400> 30

Ala Ser Gly Asn Tyr Phe Pro Gln Tyr Pro Glu Tyr Ala Ile Glu Thr  
 1 5 10 15

Ala Arg Leu Arg Thr Phe Glu Ala Trp Pro Arg Asn Leu Lys Gln Lys  
 20 25 30

Pro His Gln Leu Ala Glu Ala Gly Phe Phe Tyr Thr Gly Val Gly Asp  
 35 40 45

Arg Val Arg Cys Phe Ser Cys Gly Gly Gly Leu Met Asp Trp Asn Asp  
 50 55 60

Asn Asp Glu Pro Trp Glu Gln His Ala Leu Trp Leu Ser Gln Cys Arg  
 65 70 75 80

Phe Val Lys Leu Met Lys Gly Gln Leu Tyr Ile Asp Thr Val Ala Ala  
 85 90 95

Lys Pro Val Leu Ala Glu Glu Lys Glu Glu Ser Thr Ser  
 100 105

The paragraph at page 8, lines 20-30 has been replaced with the following amended paragraph:

--**Fig. 6.** Schematic diagram showing sequence alignment of the N-terminal peptides from Hid (SEQ ID NO:15), Grim (SEQ ID NO:16), Reaper (SEQ ID NO:17) and Smac (SEQ ID NO:18) (**Fig. 6a**) and of the BIR domains from DIAP1-BIR2 (SEQ ID NO: 30 [18]), DIAP-BIR1 (SEQ ID NO:19), XIAP-BIR3 (SEQ ID NO:20), XIAP-BIR2 (SEQ ID NO:21), XIAP-BIR1 (SEQ ID NO:22), and survivin (SEQ ID NO:23) (**Fig. 6b**). The zinc-chelating residues are shown in red whereas the conserved amino acids are highlighted in yellow. Red and yellow arrows identify those residues that make intermolecular hydrogen bonds using their side chain and main chain atoms, respectively. The solvent accessibility for the peptides (Fig. 10a) and the secondary structural elements for the DIAP1-BIR2 domain (Fig. 10b) are indicated below the sequence alignment.--

The paragraph at page 10, lines 12-19 has been replaced with the following amended paragraph.

--Fig. 13. Effect of *Drosophila* pentapeptides, Hid-5, Reaper-5, and Grim-5 on XIAP inhibition on caspase-3 activation. **Fig. 13a**, The amino acid sequences of Smac-5 (SEQ ID NO:24 [25]) and the NH<sub>2</sub>-terminal sequence of Hid (SEQ ID NO:26), Reaper (SEQ ID NO:27) and Grim (SEQ ID NO:28) are shown. The conserved pentapeptide sequences are boxed. **Fig. 13b**, 10-1000  $\mu$ M of pentapeptides as indicated were assayed in a reaction containing recombinant human Apaf-1 and procaspase-9, XIAP, purified cytochrome c, and in vitro translated <sup>35</sup>S-labeled procaspase-3. The procaspase-3 cleavage activity was measured by phosphorimaging.--